



UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/879,859	06/12/2001	Nanda D. Sinha	2733.1003-001	3484

21005 7590 07/20/2005

HAMILTON, BROOK, SMITH & REYNOLDS, P.C.
530 VIRGINIA ROAD
P.O. BOX 9133
CONCORD, MA 01742-9133

EXAMINER

RILEY, JEZIA

ART UNIT	PAPER NUMBER
----------	--------------

1637

DATE MAILED: 07/20/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/879,859	Applicant(s) SINHA, NANDA D.	
	Examiner Jezia Riley	Art Unit 1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 09 June 2005.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1,2,6-10,12-25,29-33,35-48,52-67,71-77 and 79-97 is/are pending in the application.
- 4a) Of the above claim(s) 1,24,47 and 66 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 2,6-10,12-23,25,29-33,35-46,48,52-65,67,71-77 and 79-97 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☒ Claim(s) 1,2,6-10,12-25,29-33,35-48,52-67,71-77 and 79-97 are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Response to Remarks

1. Applicants' arguments, filed on 6/9/05, have been approved and entered. They have been fully considered. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either newly applied or reiterated. They constitute the complete set presently being applied to the instant application.

Claim Rejections - 35 USC § 102

2. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

3. Claims 2, 6, 8-10, 14, 15, 18-22, 25, 31-33, 37-45, 48, 52, 54-64, 71, 72, 75-77, 79, 81, 82, 85-97 are rejected under 35 U.S.C. 102(b) as being anticipated by Sinha (Nucleic Acids Research, Vol.12, 1984, p4539-4557).

Sinha et al discloses deprotection of a synthetic oligonucleotide. Cleavage of the oligo from the polymer support (CPG page 4544), deacylation and deprotection of β -cyanoethyl group from the phosphate triester moiety can be performed in one step with concentrated aqueous ammonia (see abstract).

They disclose using a hindered primary amine tBuNH₂/pyridine mixture for the removal of β -cyanoethyl group prior to contacting with an aqueous basic solution (conc. Aqueous NH₃). The NH₃ solution is viewed as the instant aqueous basic solution and the hindered primary amine tBuNH₂/pyridine mixture is viewed as organic solvent and scavenger of instant claim 3. (page 4546). Page 4545 shows oligo sequences comprising at least 50% of combined thymine and Guanine. Further the result solution after adding the NH₃ solution to the tBuNH₂/pyridine mixture is viewed as a solution comprising aqueous NH₃ and t-butylamine and therefore is viewed to be inclusive of instant claims 48 and 49.

4. Response to arguments:

Applicants argue that the reference does not the use of hindered primary aliphatic amine in aqueous basic solution. This is not convincing because as stated in the rejection, the reference discloses: cleavage of the oligo from the polymer support (CPG page 4544), deacylation and deprotection of cyanoethyl group from the phosphate triester moiety can be performed in one step with concentrated aqueous ammonia (see abstract) using hindered primary amine tBuNH₂.

Claim Rejections - 35 USC § 103

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

6. Claims 2, 6, 7-10, 14, 15, 18-22, 25, 31-33, 37-45, 48, 52-65, 71, 72, 75-77, 79, 81, 82, 85-97 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sinha (Nucleic Acids Research, Vol.12, 1984, p4539-4557) in view of Ravikumar et al. (US 6,465,628 B1).

Sinha et al. disclose using a hindered primary amine tBuNH₂/pyridine mixture for the removal of β -cyanoethyl group prior to contacting with an aqueous basic solution (conc. Aqueous NH₃). The NH₃ solution is viewed as the instant aqueous basic solution and the hindered primary amine tBuNH₂. Page 4545 shows oligo sequences comprising at least 50% of combined thymine and Guanine.

Ravikumar et al. provides an improved method for the preparation of phosphate-linked oligomers having phosphodiester, phosphorothioate, phosphorodithioate or other linkages that have significantly reduced amounts of exocyclic nucleobase adduct resulting from the products of removal of phosphorus protecting groups. (see col. 10-12 and claims).

Therefore it would have been obvious at the time the invention was made to apply the method of Sinha for the removal of protecting group from phosphorothioate

oligo analogs since Ravikumar teaches an improved method for the preparation of oligos comprising such linkages or any kind of linkages and also any oligos which can comprise any mixture of nucleobases or only thymine nucleobases.

7. Response to arguments:

Applicants argue the references do not suggest the invention because they do not disclose of hindered primary aliphatic amine in aqueous basic solution. This is not convincing because as stated in the rejections, the reference (Sinha) discloses: cleavage of the oligo from the polymer support (CPG page 4544), deacylation and deprotection of cyanoethyl group from the phosphate triester moiety can be performed in one step with concentrated **aqueous ammonia** (see abstract) using hindered primary amine tBuNH₂. Further applicant argues that the Ravikumar make no mention of hindered primary amine. However, Ravikumar mentions use of amine in the examples. Ravikumar et al. provides an improved method for the preparation of phosphate-linked oligomers having phosphodiester, phosphorothioate, phosphorodithioate or other linkages that have significantly reduced amounts of exocyclic nucleobase adduct resulting from the products of removal of phosphorus protecting groups. Therefore, in view of Sinha, the use of hindered primary amine for oligo comprising any kind of linkages will be inherently obvious.

8. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR

Art Unit: 1637

1.136(a).


A shortened statutory period for response to this final action is set to expire **THREE MONTHS** from the date of this action. In the event a first response is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event will the statutory period for response expire later than **SIX MONTHS** from the date of this final action.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jezia Riley whose telephone number is 571-272-0786.

The examiner can normally be reached on 9:30AM - 5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on 571-272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-272-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).


JEZIA RILEY
PRIMARY EXAMINER

Wednesday, July 13, 2005